EXHIBIT B

U.S. Food and Drug Administration

Remarks by:
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Commissioner of Food and Drugs

10TH ANNUAL PDA/FDA JOINT CONFERENCE

KEYNOTE ADDRESS

"STRENGTHENING THE SCIENCE BASE FOR REGULATORY DECISIONS"

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"This text contains Dr. Henney's prepared remarks. It should be used with the understanding that some of the material may have been added or deleted during actual delivery."

Good morning, it is a pleasure to be here for the tenth annual PDA/FDA Joint Conference. While I know that every conference that we do is important and covers a good range of topics, I am particularly pleased about this year's focus on science as the cornerstone of good regulatory decisions. This, of course, has been one of the themes that I have repeatedly stressed since I returned to the Agency as Commissioner last fall.

The reasoning behind this is clear-we are a science-based regulatory Agency. Therefore, as I have consistently stressed, we cannot afford not to have the best science underpinning all of our decisions. From the researcher in our food labs, to the reviewer in our drug divisions, the inspectors out in the field, or any employee articulating a new policy-all decisions should be based on the most recent scientific developments and knowledge. Confidence comes from knowing that the correct decision has been made, because it was grounded in scientific data.

One of the most obvious areas where we must have the most up-to-date information and rigorously apply our scientific skill is in the area of product review. High-tech industries are expanding at an exponential rate. Billions of dollars are being poured into research and development for new products-including those made from biotechnology, food additives, pharmaceuticals, and devices-and we cannot afford to constrain or slow the process to get safe and effective new products to patients and consumers. The Food and Drug Administration reviews and makes judgments regarding new products that are the result of cutting-edge science. We must have the capability to keep up with these scientific developments because the judgments we render depend upon it.

Our commitment to strong scientific expertise has paid off dramatically. While at certain points in recent history the Agency has been criticized for delaying the availability of medical therapies to the patients, that is clearly no longer the case.

When adequately funded through FDA's landmark prescription drug user fee program, the Agency has

proven that it can meet the challenge of extremely demanding performance goals. Drugs are now being reviewed as fast or faster than anywhere in the world, without compromising the very stringent standards that Americans and the rest of the world have come to expect.

There is a great deal of value in having a regulatory agency based on high standards, that performs reviews in a timely fashion, using open and transparent processes. For instance, our scientists and reviewers should be present to present their findings in open forums, not behind closed doors. This adds pressure to the individual decisionmaker, but ultimately benefits society by building the trust and confidence that consumers have in a system that reviews products on their behalf. This is good for patients, good for consumers, and good for the country as a whole.

We are seeing not only an increased number of new products brought to market, but also products that represent significant advances over those that were previously available. Within just the past few months, we have approved new therapies for osteoarthritis, influenza, obesity, HIV, and diabetes. We have also seen new clotting agents for patients with hemophilia A, a new imaging device for the diagnosis of breast cancer, a new device for removing blood clots from blocked arteries, and a new biological treatment for non-Hodgkin's lymphoma.

But a cautionary note, we for we need to always be cautious-we cannot be blinded by our successes. As FDA's product review times have been reduced-and after a few very high-profile product withdrawals--there has been some concern that FDA is rushing to approve drugs too fast-drugs that may cause harm to patients. Therefore, I would like to briefly discuss what I see as the Agency's approach to proper risk-based decision-making, which will be one of our greatest areas of concentration in coming years.

It is not realistic to think that the Agency can ensure that there will be no risks to patients when it approves a drug. After all, the basic safety decision is a weighing of benefits and risks, not a conclusion that safe equals no risk. One pivotal question in this discussion is how extensively drugs should be studied to uncover adverse reactions before approval. Clearly, there is less certainty with a study of 500 people than with one of 5,000 or 150,000 people. Yet, there are some risks that we won't know about from the clinical trials--some adverse events are very rare. For a side effect that would occur in 1 in 50,000 patients, a sponsor would have to study 150,000 people before the drug was approved in order to have a good chance of that risk even showing up-although, even then, there is no guarantee that it would show up. Having to study 150,000 people with each disease would be a barrier to getting drugs on the market, especially those for rare diseases.

Another reason some risks do not show themselves during clinical studies has to do with how drugs are used in the real world. In clinical trials, drugs are studied only for the use the sponsor is pursuing. They're studied in patients who are highly screened for eligibility and are carefully monitored. After a drug is out on the market, patients will usually not be as rigorously studied or monitored. In addition, they may be taking a variety of different medications-and possibly dietary supplements and other products--that could interact with the drug. And, yes, in the general practice of medicine, drugs are used for conditions other than those they were approved for. We must take all of these factors into account as we work with sponsors to try to make safe and effective products available to patients as quickly as possible.

Unlike in other areas of FDA's work, there is no set formula or standard for a determination that a product is safe. Safety is a relative term. There is a continuum of uncertainty that is tolerated, depending on the seriousness of the illness. For drugs that are meant to treat serious or life-threatening diseases--and where effective treatments are not yet available--more uncertainty is tolerated. On the other end of the continuum, a drug that is going to be sold over-the-counter for consumers to use, a very high level of certainty is expected.

Every single drug has side effects. Sometimes these will be rare, and sometimes these will not be very serious. But for every drug that we approve, we have to balance the benefits of the drug against its risks. FDA cannot make these risks go away--and we should not, as an Agency--imply that we can. We need to make clear what the risks are, and communicate that information as effectively as possible to all involved.

The majority of injuries and deaths in this country from medical products are from known side effects, not from the unexpected ones. Therefore, although it is important to evaluate FDA's standards in its premarket decision-making, it is also important to look at whether risks are managed throughout the health care delivery system and whether adequate safeguards are in place.

All participants in the medical product development and health care delivery system have a role to play in maintaining this benefit/risk balance by making sure that products are developed, tested, manufactured, labeled, prescribed, dispensed, and used in a way that maximizes benefit and minimizes risk.

Once a product is marketed, determinations about the safety of a product become the shared responsibility of health care professionals and the patients themselves. After looking at the different roles that are played in the health care system, the Agency has developed a report on risk management that assesses these different roles.

FDA makes the original risk-benefit decision about a product at the time of approval. We generally evaluate the population that would be using the drug and ask whether the benefits to that population outweigh the risks. If yes, approval of the drug is given. Once on the market, the prescriber is the primary risk manager. Physicians are expected to make rational choices on behalf of their patients as they write prescriptions and weigh the risks and benefits of the drug for each patient's particular situation. Consumers are also at times their own risk managers as they purchase over-the-counter products, weighing whether the indications for use outweigh the possible side effects.

To make improvements in our current risk management system, we need to incorporate patients into our risk management decisions much more extensively. Computers and other tools to assist prescribers in making the correct choices for their patients are now being used. Patients are the ones who are assuming the risk, and we know that different people weigh risk differently. Some patients-usually the desperately ill-are likely to assume more risk for even a minimal chance of benefit. And, patients often actively engage in minimizing their own risk by reading labels, keeping track of their medications, keeping track of the basic side effects, and, simply-but importantly--asking questions.

When adverse reactions do occur, we need to assure that there are feedback loops throughout the system so that these events can be effectively communicated and acted on appropriately. Doctors, pharmacists, and patients can report serious adverse reactions to the agency through our MedWatch system, or they can make a report to the manufacturer. "Dear Health Professional" letters may be used to inform doctors and other providers of a new safety issue. And, if the new issue really alters the risk-benefit ratio so the risks of the drug--including the newly-found risks--now outweigh the benefits, we must consider more dramatic steps can be considered, such as revising the label or black box information, or in rare instances, requiring the drug's removal from the market.

Again, even as we plan our strategies for risk-management along the entire health care continuum, one of the most central parts of the process is the review decision made by the Agency. Therefore, it is critical that the Agency have the knowledge and experience needed to face the new science and technology that is coming before it in product applications.

How does the FDA intend to maintain its ability to keep pace with new science and technology? Let me discuss a few ways in which we are addressing this question. My first area of focus is on luring the top scientists in the country to our Agency--and keeping them with us. As I travel around the country to academic or industrial sectors, I consistently remind scientists that there are extremely rewarding careers available in government agencies such as ours.

It is critical that we invest wisely in those individuals that we recruit and retain for these tasks that are so fundamental to effective protection of the public health. Measures such as ensuring that more training opportunities, research grants, cooperative agreements, and fellowships are just some of the programs that are made available to our employees.

We need attention and resources, but time money, to provide training and retraining of our scientists to help ensure that they have state-of-the-art knowledge of new scientific developments and new product technology is essential for us to remain a credible, science-based agency. We are identifying opportunities for our scientists to work in areas involving research and technology in other settings, such as with industry, academia and other governmental agencies, academia, and-where appropriate--industry. By having these kinds of educational opportunities open to our scientists, we ultimately enable them to bring back to the Agency deeper knowledge that translates into better and more efficient performance of regulatory tasks.

We are also awarding new research and risk assessment grants and establishing new procedures to better plan and coordinate research among Federal partners; we have funded seven cooperative agreements totaling $1 million, including research partnerships with Washington State University, New England Medical Center, the University of Georgia, and the University of Wisconsin.

These research and testing efforts demonstrate the success that can be achieved when government agencies work together and seek help from our colleagues in academia and industry. Such collaborations include: work on studies designed to evaluate the carcinogenicity of fumonisin B1, a mycotoxin produced by the fungus *Fusarium moniliforme*, one of the major species found in corn and corn products, and to provide data on the mode of action of toxicity and carcinogenicity to facilitate the process of risk assessment; and development of new protein-based mass spectral techniques to investigate properties of bacteria such as antibiotic resistance and acid or heat resistance.

By using these types of agreements and collaborations with scientists outside of the FDA, we are effectively leveraging the resources and expertise of outside entities. This allows us to stretch our limited resources a bit further, and to harness a greater breadth of experience within the scientific community. By collaborating with those outside the Agency, we are able to attain a wide range of perspectives, further ensuring that all of our decisions are grounded in good science.

By enhancing our scientific infrastructure in the many ways that I have mentioned, we are truly bringing FDA into the twenty-first century. I look forward to the exciting future of this Agency, the role that science and technology will play in it, and our work together in those areas. For in the words of Eden Phillpotts, "The universe is full of magical things patiently waiting for our wits to grow sharper." Therefore, I wish you great success during this conference, and I hope that your wits are sharpened over the few days. Thank you very much.

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